APPLICANT:	M. Pamela Griffin, et al.	ART UNIT:	3762
SERIAL NO.	09/770,653	EXAMINER:	Frances P. Oropeza
FILED:	January 29, 2001	CUSTOMER NO.:	34444

TITLE: Method and Apparatus for the Early Diagnosis of Subacute, Potentially Catastrophic Illness

AFFIDAVIT UNDER 37 CFR § 1.132

Commissioner for Patents
PO Box 1450, Alexandria,
VA 22313-1450

Sir:

I, Boris P. Kovatchev, declare and state as follows.

1. I am Associate Professor of Psychiatric Medicine and Health Evaluation Sciences at the University of Virginia.

2. I have Ph.D. in Mathematics from Sofia University, Sofia, Bulgaria, 1989.

3. A listing of my education, publications, projects, awards, and work history are provided in my Curriculum Viate in the attached Appendix.

4. I am familiar with the prosecution of the above-identified Application.

5. In response to the pending rejections of the claims in this case under 35 U.S.C. § 102(b) as being anticipated by Gordon et al U.S. Patent No. 4,862,361 (hereinafter "Gordon") and 35 U.S.C. § 103 over Gordon in view Schroeppel et al U.S. Patent No. 6,035,233 (herein after "Schroeppel"), I submit the following data:

6. Gordon and/or Schroeppel fails to teach or suggest the following of the present invention:

i) A method for early detection of subacute, potentially catastrophic illness in an infant, as recited in base claim 39, which calls for:

(a) monitoring frequency histograms of RR intervals in the infant;

(b) identifying at least one characteristic abnormal pattern or distribution; and

(c) correlating the at least one abnormal pattern or distribution with said illness.

ii) An apparatus for early detection of subacute, potentially catastrophic infectious illness in a patient, wherein the patient is an infant, a newborn infant, a toddler, or a child, the apparatus, as recited in base claim 69, which calls for:

(a) a monitoring device, continuously monitoring frequency histograms of RR intervals in the patient; and

(b) a microprocessor, identifying at least one characteristic abnormal pattern or distribution in the RR intervals that is associated with the illness.

7.

a. INTRODUCTION

For purpose of introduction of the prior art, Gordon U.S. Patent No. 4,862,361 (hereinafter "Gordon") teaches real-time monitoring of power spectra of heart rate time series. Thus, a difference between Gordon et al and the present invention is fundamental. Specifically, Gordon et al. use prevalence of various HR frequencies to anticipate illness. Thus, Gordon et al use patterns of *temporal regularity* (frequency) shifting from one state to another. In other words, they state that in health a certain frequency region (regularity of HR) is dominant, while in illness another frequency region (regularity of HR) becomes dominant (with respect to respiratory rate). Therefore Gordon et al rely on micro-level (beat-level) temporal regularity of HR, shifting to another micro-level temporal regularity, to detect illness.

In contrast, the present invention quantifies micro-level (beat-level) *temporal irregularity*. No stable frequencies for any period of time are required to perform these

analyses. Therefore the present invention would work in situations when Gordon et al analyses fail (e.g. when there are no apparent periods with certain dominant frequencies).

In short, the present invention has not only a fundamentally different mathematical approach, which does not follow from Gordon's work, but is also based on a fundamentally different physiology underlying HR changes prior to illness. While Gordon's frequency shifts indicate changes in relative parasympathetic-to-sympathetic activity, reduced irregularity of RR intervals proposed by the present invention indicates greater system isolation and disruption of internal conduits and control mechanisms.

Thus, the present invention describes real-time monitoring of other kinds of physiology of heart rate. Unlike Gordon, the present invention analyses do not calculate modified or unmodified power spectra or any other frequency-domain parameter, and therefore uses entirely different mathematics and approach.

b. RECONSIDERATION

i. In particular, the Office Action (par. 2, page 3) states that Gordon discloses:

...a tachometer waveform and by using the respiratory peak within a peak and judging the value against a value of two standard deviations from the mean.

The Applicants' present invention neither calculates a tachometer waveform, nor does it calculate a respiratory peak to be judged against two standard deviations above the mean.

ii. In particular, the Office Action (par. 2, page 3) states that Gordon discloses:

... the R-R intervals are measured, collecting 1024 points (a ten to the third order data set), and third moment and higher data set is created

The Applicants' submit that Gordon invention does not calculate third or higher moments of the heart rate data, as described in the present invention. The Gordon invention mentions calculations of the variance, or second moment, of the RR intervals (c16). This is exclusively in the context of correcting artifacts in the data, and not for interpretation of the clinical status of the patient as in the present invention.

iii. The Applicants' submit that the methods taught by Gordon are different than the

Applicants' claimed invention. Gordon teaches a frequency domain analysis of a tachometer waveform. The Applicant's claimed invention provides a mathematical analysis based on frequency histograms of the RR intervals. Following Gordon et al, it is impossible to arrive at the present inventions' concept of micro-level temporal irregularity because all Gordon analyses are based on a Fourier transformation of the data, which mathematically eliminates the time axis from the data, leaving only frequency (or period) vs. count (power) axes. The very mindset of all Fourier-based analyses is looking what happens at specific repeated (and therefore temporally regular) points of the data, not looking at irregularity over time. It is a mathematical impossibility to arrive at any irregularity characteristics as Gordon teaches, e.g. using Fourier analysis - when the data is irregular Fourier analysis would produce a flat spectrum, which yields no information.

8. Moreover, the Examiner's reliance on Schroeppel does not supply the deficiencies of the Gordon disclosure.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like so made punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code that such willful false statements may jeopardize the validity of the application of any patent issued thereon.

Date: March 16, 2004

B. Kovatchev

Boris P. Kovatchev